CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
TRICHLOROMELAMINE

Chemical Code # 001023, Tolerance # 51006
SB 950 # 919

Original date: January 31, 2001; revised October 19, 2001 and April 2, 2002

I. DATA GAP STATUS

Chronic toxicity, rat: Subchronic, rat	Data gap, inadequate study, no adverse effect indicated. Unacceptable study on file
Chronic toxicity, dog:	Data gap, inadequate study, no adverse effect indicated.
Oncogenicity, rat:	Data gap, no study on file.
Oncogenicity, mouse:	Data gap, inadequate study, no adverse effect indicated.
Reproduction, rat:	Data gap, no study on file.
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, possible adverse effect
Chromosome effects:	No data gap, possible adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 185661 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
Compiled by J. Kishiyama and J. Gee, 1/31/01; revised by Gee, 10/19/0 and 4/2/02.
File name: T020402

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

NOTE: Trichloromelamine is used as a sanitizer to produce chlorine. The major potential residue is melamine. The toxicology of melamine was discussed in the Risk Characterization Document for the active ingredient, cyromazine, dated 1993, for which melamine is also a product. A number of the studies in this Summary of Toxicology Data for trichloromelamine were conducted with melamine. This is noted in the 1-liner for each study. (Gee, 1/31/01)

21 CFR 178.1010, p. 336 of the 4/1/99 edition, lists sanitizers containing trichloromelamine as on the "Indirect food additives: adjuvants, production aids, and sanitizers". (Gee, 10/16/01)

GENERAL CITATIONS

51006-005 115385 An explanation from Weinberg Consulting Group, Inc., Washington, D. C., why the US EPA should not require further testing with trichloromelamine, dated August 15, 1987. The petition covers chemistry, use as a sanitizer, brief comments on studies with melamine (the likely residue), and estimates of dermal absorption. A response by E. F. Tinsworth, Director, from US EPA, dated August 4, 1988, concluded that no additional toxicology data were required. No worksheet. (Gee, 1/25/01)

51006-020 182659 Appendices for M. S. Weinberg document of 8/15/87. Part 1 contains 11 subdivisions. Some of the contents appear to be duplicates of earlier submissions. None are laboratory studies of toxicological effects. Part 2 contains a duplicate of the Food Additive Petition and of the interim and final reports for the rat and dog studies conducted at Hazleton in the 1950's. See summaries of those studies below. (Gee, 10/15/01)

51006-005 115386 Leifheit, B. A. "Product Chemistry for trichloromelamine, technical grade" (9/14/90). The last section under this record number consists of the response of US EPA to Phase 2 submissions regarding EPA decisions for trichloromelamine but was not dated. Many of the test types were given a "decide in phase 4" conclusion. No worksheet. (Gee, 1/25/01)

51006-006 115388 Sections of a petition regarding trichloromelamine consisting of chemistry, use, residues, efficacy, and analysis. No worksheet. (Gee, 1/25/01)

51006-006 115390 Very brief summaries of acute and chronic toxicity. No worksheet. (Gee, 1/25/01).

51006-006 115395 "Report on melamine: Acute and chronic toxicity" (American Cyanamid Co., report 55-21, 6/15/55) Brief summary of acute and chronic toxicity of melamine. (Gee, 1/26/01)

51006-007 115396 Copies of patent documents regarding melamine. No worksheet. (Gee, 1/26/01)

51006-007 115399 "Melamine" (IARC Monographs, volume 39, 333-346, 1986) A summary of chemistry, uses, and toxicity. The study sponsored by NTP using Fischer 344/N rats and $B6C3F_1$ mice was summarized. The presence of urinary bladder stones at high dietary doses in mice and rats was discussed. No worksheet. (Gee, 1/29/01)

51006 - 019 182658 This record number contains multiple documents which address several topics. Section A: This section contains copies of the US EPA reviews of three genotoxicity studies which were evaluated as "upgradeable" in the initial review by Medical Toxicology Branch. Contained in the EPA review is the purity of lot 1933 as 95.9%. This information was not included in the Hazleton reports. Presumably, the purity of the lot was found elsewhere in the submissions for trichloromelamine. This information upgrades three studies found in records 128842, 128854 and 128874, filling the data gaps for 842, 843 and 844 test types. Section B contains the US EPA "Reregistration Status Report Card" from 1995. According to the list of guideline required studies, US EPA has accepted a 90-day feeding study (MRID 43064301) and has waived the requirements for chronic rodent and non-rodent studies, and rat and mouse oncogenicity studies. Note that the registrant has requested that DPR waive these same studies and the rat reproductive study. Section C is a duplicate of record 115385, the response by Weinberg Consulting Group prepared in 1987. This response outlines why EPA should not require further studies for trichloromelamine. Supplemental information. (Gee, 10/12/01)

51006-021 182660 This record contains a waiver request, risk assessment and other documents. The volume contains 9 subdivisions, as follows: A waiver request for the 90-day feeding study with dogs, including an estimate of exposure from use as a sanitizer; a copy of a US EPA review of an acute oral study in rats (category II); a 1-page summary from Hazleton of eye irritation scores in rabbits, showing severe irritation; US EPA documents for acute studies giving toxicity categories for acute dermal (III), eye irritation (I), dermal irritation (I) and as a non-sensitizer with CORE classifications of minimum for the studies; several pages of data from Hazleton for an acute dermal study in rabbits with some animals still showing effects at day 21; 22 of 44 pages of an acute oral study in rats from Hazleton, 1994; a Phase 2 14-day range-finding study and a 90-day oral feeding study in rats from the U.S. Army Environmental Hygiene Agency, 1989; a copy of the US EPA review of the 90-day study as CORE Minimum; and a brief report from the Biological Test Center, 1995, entitled "Determination of the trichloromelamine residue on bar glasses sanitized with Beer Clean® Sanitizer", J. A. Fruetel, author. Supplemental information. (Gee, 10/15/01)

CHRONIC TOXICITY, RAT

001 045328 "Data for trichloromelamine, petition section E." Brief summary of a study by Wallace and Tiernan, 1949. Female rats were fed whole-wheat diets supplemented with 0, 10, 100 or 1000 ppm trichloromelamine [10/group ?] for 14 months. There was no affect on body weight (only data presented). No worksheet. Unacceptable, not upgradeable. (Gee, 1/30/01)

001 045329 "Data for trichloromelamine, petition section E." One paragraph summary of a 2-year study with rats fed 1000 ppm [melamine ?]with no affect on food consumption, growth or mortality. No worksheet. Unacceptable, not upgradeable. (Gee, 1/30/01)

006 115394 Gray, E. H. "Chronic Feeding - Rats". Final report. (Hazleton Laboratories, November 27, 1953). Melamine (purity not given) was admixed with the feed at concentrations of 0, 0.1 and 1.0% (10,000 ppm) and fed to 10 albino rats/sex/group during a two-year study. Hematology with limited parameters was conducted on 3/sex/group only. Clinical chemistry was very limited as was urinalysis. No ophthalmology was included. Body weights were lower in high dose males. In the second year in all groups, there was evidence of respiratory involvement. All animals were necropsied but only a limited list of tissues was preserved/examined. This list did not include such tissues as eyes, brain, pituitary, prostate, others. The only organ examined for all animals was the urinary bladder. Urinary bladder changes were reported for 1.0 % males and females and consisted of epithelial hyperplasia and benign papilloma, and calculi. Apparent NOEL = 0.1%. UNACCEPTABLE. Not upgradeable. Insufficient data to identify any possible adverse effect for melamine. Major deficiencies included test article was not trichloromelamine, inadequate number of animals and doses, concurrent disease. (Kishiyama and Gee, 1/26/01).

Note: 006 115395 gives the approximate dosages as 0.08 and 0.75 g/kg for 0.1 and 1.0% diets.

51006- 006 115391. Progress report of rat feeding study, dated May 1, 1952. A second progress was dated December 3, 1952, superceding the earlier one. Page 17 has a progress report for a feeding study with dogs, dated December 13, 1952.

001 045331 Duplicate of 115391, progress report of May 1, 1952.

001 045332 Duplicate of 115391, December 3, 1952 progress report.

001 045335 Summary of 115391.

001 045336 Duplicate of study 115391, final report.

001 045339 One paragraph summary of record 115394. No worksheet. (Gee, 1/30/01)

001 045343 Brief version of study in record 115394. No worksheet. (Gee, 1/30/01)

SUBCHRONIC, RAT

51006 - 022 185661 Michie, M. W. "Trichloromelamine - 90-Day Subchronic Study in Rats". (U. S. Army Environmental Hygiene Agency, Tier One Toxicological Study No. 75-51-0743-88, 1/17/89.) Trichloromelamine (technical, 92.07 %)was administered daily via oral gavage at doses of 0, 0 (Triton X-100 in distilled water), 30, 150, 300 mg/kg/day for 90 days to 10 Sprague-Dawley rats/sex/group. Doses were given 5 days per week at a concentration of 75 mg/ml, with volumes adjusted to deliver the dose. Food consumption was reduced slightly for high-dose females. Body weight gain and body weight were lower for the high-dose groups. RBC counts were lower for high-dose males and calcium concentration in blood was lower for mid and high-dose females. Congested breathing was notable and hemorrhagic erosion of the stomach mucosa was noted for non-surviving mid and high-dose animals. Mortality occurred in the mid dose group (3/10 females) and high dose groups (4/10 males and 4/10 females). Microscopic findings included hyerplasia of the stomach, tracheitis and blood congested major organs for mid and high-dose groups, considered treatment related. The dosing material had a pH of 4 and may have been a contributing factor. NOEL = 30 mg/kg/day. UNACCEPTABLE (no ophthalmology) but otherwise adequate. Not upgradeable. No adverse effect. (Kishiyama and Gee, 3/29/02)

Note: This 1-liner is replaced by the one above for record 185661.
51006 - 021 182660 (821) " Phase 2 toxicological study No. 75-51-0743-88 (2) trichloromelamine 14-day range finding and 90-day subchronic studies in rats, 3 August 1988 - 17 January 1989." (M. Michie and R. A. Angerhofer, U. S. Army Environmental Hygiene Agency, 11/13/92) Trichloromelamine, technical grade [92.07%] [items in brackets were taken from the US EPA review of the study], was given by oral gavage to Sprague-Dawley rats for either 14 days or 90 days. 14-day range finding study: Six/sex were given 0 (water), 25, 50, 100, 200, 400, 800 or 1600 mg/kg/day for fourteen consecutive days. Deaths occurred at ≥ 400 mg/kg/day. Clinical signs were seen in all groups (no data). Lung changes were seen in all treated groups with no dose response, possibly associated with the foaming of the dosing material. Subchronic study: Ten/sex were given doses of 0 (water), 0 (0.08% Triton X-100 surfactant), 30, 150 or 300 mg/kg/day over 90 days. Body weight at the high dose was occasionally statistically lower with an overall lower weight gain. The major findings were histopathological lesions in the non-glandular portion of the stomach [3/9 high dose males and 1/7 mid dose males and 1/9 high dose females]. These lesions were moderate hyperplasia and chronic inflammation. NOEL = 30 mg/kg/day. All appendices were missing. Report is incomplete. Ophthalmology apparently was not conducted. Study may possibly be upgraded with the submission of the complete report, a statement clarifying the dosing regimen (days/week), and whether eyes were examined at necropsy. UNACCEPTABLE (Gee, 10/16/01). Note: The review of this study by US EPA, 9/21/94, was included in -021, section VII. Their conclusion was that the study was Core minimum.

CHRONIC TOXICITY, DOG

006 115393 T.W. Tusing. “Chronic Feeding - Dogs”. (Hazleton Laboratories, November 27, 1953). Precipitated and crystal melamine were admixed in the feed, each at a concentration of 3% (30,000 ppm) and fed for 1 year to 1 male and 2 female mongrel dogs per group. Hematology and clinical chemistry were limited in the parameters measured. No ophthalmology was performed. Histopathology was very limited in conduct and reporting. No food consumption or water intake data were reported. The major findings reported were for urine changes of lower specific gravity, increased urine output, melamine crystalluria (crystal melamine only) and protein and occult blood. Data for body weight and melamine intake, limited hematology parameters and urinalysis for individual dogs were all the data that were reported. Histopathology findings were given in text form. A number of the dogs had worm infestations. UNACCEPTABLE . Not upgradeable (multiple deficiencies including test article not being the registered active ingredient of trichloromelamine, single dose level). (Kishiyama and Gee, 1/26/01).

001 045334. Same study as 115391 without Table 618.

001 045330 “”Data for trichloromelamine, petition section E.” One paragraph summary of a 1-year study in which dogs were fed 30,000 ppm melamine. Apparently the same study as record 115393. No worksheet. (Gee, 1/30/01).

001 045333 Progress report of December 18, 1953 for record 115393.

001 045338 One paragraph summary of record 115391 with melamine.

001 045342 Brief report for study in record 115393 with melamine at 3% of the diet. No worksheet. (Gee, 1/30/01)

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

008 128875 Morrissey, R. L. "Strain A Mouse Lung Tumor Bioassay (Shimkin Mouse Test) of Trichloromelamine". (Pathology Associates, Inc., PAI Study No. 87042, November 3, 1988.) Trichloromelamine (lot 1933, purity not stated) at concentrations of 0 (tricaprylin), 1.04, 2.60, and 5.21 mg/kg was administered by I.P. injection 3 times per week for 8 weeks to 16 A/J mice/sex/group, followed by 16 weeks of observations before sacrifice. The emphasis was on lung pathology. Trichloromelamine treatment did not significantly increase the incidence of lung lesions. No other evidence of oncogenicity with Trichloromelamine treatment was reported. UNACCEPTABLE (supplemental study to evaluate potential for oncogenicity in lungs – not a FIFRA guideline study protocol). Not upgradeable. No adverse effect identified. (Kishiyama and Gee, 1/29/01).

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

** 009 136110 Tyl, R. W., M. C. Marr, C. B. Myers. "Developmental Toxicity Evaluation of Trichloromelamine Administered by Gavage to CD® (Sprague-Dawley) Rats." (Research Triangle Institute, RTI Identification Number 65C-5742-100/200, April 10, 1995.) Trichloromelamine (lot 2107, 94.4%) was administered by gavage at doses of 0 (corn oil), 62.5, 125, 250, or 500 mg/kg/day to 25 mated female CD® (Sprague-Dawley) rats/group during gestation days 6 through 15. Mortality was 7/25 and 1/25 for the 500 and 250 mg/kg/day groups, respectively. Clinical effects were observed in the two higher dose groups, including lethargy, gasping, salivating and chromodacryorrhea, with an occasional sign in the lower dose groups. Body weight and body weight change were significantly reduced for the 500 mg/kg group. Food consumption was reduced on occasion for all groups, except the 125 mg/kg group. Maternal NOAEL = 62.5 mg/kg/day. No adverse fetal developmental effects were reported. Developmental NOEL $\geq$ 500 mg/kg/day. ACCEPTABLE. No adverse effect. (Kishiyama and Gee, 1/30/01).

51006-007 115398 "Effect of 2,4,6-triamino-"S"-triazine (TR), 2,4,6 "tris" (ethyleneimino)-"S"-triazine (TEM) and N,N',N''-triethylenephosphoramide (TEPA) on rat litter *in utero*" (J. B. Thiersch, published in: Proc. Soc. Exp. Biol. Med. 94: 36-40 (1957), Univ. of Washington School of Medicine, Seattle) Melamine (TR, purity not given) was given to pregnant rats (strain unclear) by intraperitoneal injection, 70 mg/kg, on days 4, 5 or 7, 8 or 11, 12 of gestation with day of massive sperm findings being day 0. Females were approximately 6 months old and had delivered one previous litter. Groups contained 21, 26 and 26 rats with increasing days of gestation. Parameters measured included weight gain, total implants, live and dead fetuses and resorptions, average litter weight, and average fetal weight and length. No statistically significant

findings were reported with melamine. [Both TEM and TEPA had possible adverse effects.] No worksheet. SUPPLEMENTAL. (Gee, 1/26/01).

TERATOLOGY, RABBIT

** 010 136111 Tyl, R. W., M. C. Marr, C. B. Myers. "Developmental Toxicity Evaluation of Trichloromelamine Administered by Gavage to New Zealand White Rabbits." (Research Triangle Institute, RTI Identification Number 65C-5742-300/400, April 10, 1995.) Trichloromelamine (lot 2107, 94.4%) was administered by gavage at doses of 0 (corn oil), 30, 60, 90, or 120 mg/kg/day to 16 mated female New Zealand White rabbits/group during gestation days 7 through 19. Trichloromelamine treatments reduced food consumption and body weight change in all dose groups, days 7 – 9 of exposure. Food consumption was also significantly reduced days 9 - 12 at 90 and 120 mg/kg/day. Maternal NOEL = <30 mg/kg/day. No developmental toxicity reported. Developmental NOEL = >120 mg/kg/day. ACCEPTABLE. No adverse effect. (Kishiyama and Gee, 1/30/01).

GENE MUTATION

**** 008 128842** Jagannath, D. R. "Mutagenicity Evaluation of Trichloromelamine, Lot #1933, Dorex, Inc. in the Ames *Salmonella*/Microsome Reverse Mutation Assay. Final report." (Hazleton Laboratories America, Inc., HLA Project No.: 20988, January, 1987.) Trichloromelamine (lot 1933, purity not stated) was evaluated for mutagenicity at concentrations of 0 , 0.10, 0.25, 0.50, 1, 2.5, 5, 10, and 25 µg/plate using *Salmonella typhimuriun* strains TA 1535, TA 1537, TA1538, TA 98, and TA 100, triplicate plates, two trials with TA98 and TA100, with and without rat liver activation. Trichloromelamine without S9 mix more than doubled the number of revertants in the initial and repeat assay with TA98 only. Possible adverse effect. Initially evaluated as unacceptable but upgradeable (test article purity) (Kishiyama and Gee, 1/29/01) Information supplied in 182658 for purity of 95.9 % upgrades the study to ACCEPTABLE status. (Gee, 10/12/01)

008 128846 Cifone, M. A. "Mutagenicity of Trichloromelamine in a Mouse Lymphoma Assay. Final report". (Hazleton Laboratories America, Inc., HLA Project No.: 20989, November, 1986.) Trichloromelamine (lot 1933, purity not given) at concentrations ranging from 7.50 to 50 µg/ml without metabolic activation and from 10.0 to 60 µg/ml with rat liver metabolic activation was evaluated for mutagenic potential with mouse lymphoma L5178Y cells, 4 hours exposure, 2-day expression period. Single trial with and without activation. Trichloromelamine treatment did not significantly induce mutation frequency. UNACCEPTABLE, not upgradeable (no purity of test material, single trial). (Kishiyama and Gee, 1/29/01).

008 128876 Brusick, D. "Mutagenicity Evaluation of Sample B Trichloromelamine. Final report". (Litton Bionetics, Inc., LBI Project No. 2683, October 26, 1976.) Trichloromelamine (no lot number, no purity) was evaluated for mutagenicity at concentrations of 0 (water) , 0.10, 1, 10, 100 and 500 µg/plate with and without rat liver metabolic activation (S9 Mix) and using *Salmonella typhimurium* strains TA 1535, TA 1537, TA1538, TA 98, and TA 100 and *Saccharomyces cerevisae* strain D4, single plate per concentration, single trial. Trichloromelamine treatment with and without S9 Mix did not significantly increase the number of revertants for either *Salmonella* or *Saccharomyces*. UNACCEPTABLE (major deficiencies). Not upgradeable. No adverse effect identified. (Kishiyama and Gee, 1/29/01).

MELAMINE

51006-007 115400 "Salmonella mutagenicity test results for 250 chemicals." (Haworth, S., T. Lawlor, K. Mortelmans, W. Speck and E. Zeiger, publ. in: Environmental Mutagenesis, Supplement 1: 3-142 (1983)) Melamine (no purity given) was one of the chemicals tested at Case Western Reserve using *Salmonella* strains TA1535, TA1537, TA98 and TA100 with a 20 minute pre-incubation step. Both hamster and rat liver S-9 fractions were used. Concentrations were 0 to 111 mg/plate, selected in a preliminary assay with TA100. Results were negative (page 108 and Table I). No worksheet. SUPPLEMENTAL (test material not the registered active ingredient) (Gee, 1/29/01).

CHROMOSOME EFFECTS

**** 008 128854** Murli, H. and J. L. Ivett. "Clastogenic evaluation of trichloromelamine in an *In Vitro* Cytogenetic Assay Measuring Chromosomal Aberration Frequencies in Chinese Hamster Ovary (CHO) Cells. Final report." (Hazleton Laboratories America, Inc., HLA Project No.: 20990, December, 1986.) Trichloromelamine (lot 1933, purity not stated) was evaluated for the potential to induce chromosomal aberrations in Chinese hamster ovary cells (CHO) at concentrations ranging from 0 (ethanol), 7.5 to 60 µg/ml and 10 to 75 µg/ml without and with rat liver metabolic activation, respectively. There were duplicate cultures per concentration and two trials. The percentage of cells with aberrations was significantly increased with trichloromelamine at high doses without and with metabolic activation, which were not excessively cytotoxic. Possible adverse effect. Initially evaluated as unacceptable (purity of test material was not given) but upgradeable. (Kishiyama and Gee, 1/29/01). Submission of the purity as 95.9% upgrades the study to ACCEPTABLE. (Gee, 10/12/01)

008 128878 Hupka, A. L., R. Davis, and I. Gray. "Determination of the Acute Oral LD_{50} and Dominant Lethal Effects of Trichloromelamine in Mice". (Omni Research, Incorporated, Contract No. DAAD-05-87-C-0095, January 31, 1989.) Trichloromelamine (lot# UN1479, no purity stated) was administered in a single gavage dose at 800, 1000, 1200, 1600 or 2000 mg/kg to CF-1 male mice to determine the LD_{50}. Males were observed for an additional 14 days. There were 4 per dose in the first trial and 6 in the second for a total of 10 male mice/dose. LD_{50} = 1495 mg/kg (95% confidence interval 1196 – 1869 mg/kg). No clinical signs were reported at any dose. In the dominant lethal study, male mice were given 0 (sterol diluent), 30, 150 or 300 mg/kg for 5 consecutive days. There were ten males per treatment group and 20 in controls. Positive control was triethylenemelamine (TEM), given as a single intraperitoneal dose to 10 males. Mice were mated to 2 untreated females each week over 8 weeks. Females were examined for fertility, implantations, early and late fetal death of implants. No adverse effect on any of the parameters measured in the females. No effects on male body weights and no clinical signs in treated males. UNACCEPTABLE . Not upgradeable (insufficient number of males per group for dominant lethal portion, no analysis of dosing material for stability and content).
(Kishiyama and Gee, 1/30/01)

DNA DAMAGE

** 008 128874 Cifone, M. A. " Evaluation of Trichloromelamine in The Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay. Final report." (Hazleton Laboratories America, HLA Project No.: 20991, January, 1987). Trichloromelamine (lot 1933, purity not stated) at

concentrations ranging from 0 (acetone), 5.11 to 30 µg/ml was evaluated for DNA damage/repair with primary rat hepatocytes. Trichloromelamine did not induce significant changes in the nuclear labeling of primary rat hepatocytes. Initially evaluated as unacceptable but upgradeable (individual data, purity of test material, discussion of acetone as vehicle). (Kishiyama and Gee, 1/29/01) Submission of the purity as 95.9% upgrades the study to ACCEPTABLE status. (Gee, 10/12/01).

OTHER SUPPLEMENTAL INFORMATION

51006-007 115397 Weeks, M. H. and T. B. Weyandt "Preliminary assessment of the relative toxicity of candidate disinfectant, food service (chlorine-iodine type) NSN 6849-00-810-6396 and trichloromelamine" (Study no. 75-51-0195-84. United States Army Environmental Hygiene Agency, Aberdeen Proving Ground, 11/83). The purpose of the studies was to evaluate acute effects of a disinfectant procedure for mess gear in the field when hot water was not available. One of the components in Pouch A was 10% trichloromelamine, part of the chlorine producing formulation. Pouch B contained KI. Trichloromelamine was tested in a series of standard acute toxicity studies as a dry material and as a wet paste (distilled water). The results were summarized. 1. Skin irritation study with NZW rabbits, 24 hours: 0.5 gm dry white powder, very slight irritation, category IV and 0.5 gm wet paste, moderate irritation, III. 2. Eye irritation in rabbits, washed after 20 seconds: 0.1 gm dry white powder, unwashed, corrosive, I, and washed, moderate reversible injury, II. 3. Acute oral toxicity in rats with water as vehicle and administered by gavage at 500 mg/ml: LD50 of 690 mg/kg (560 – 870 mg/kg), III. 4. Acute dermal toxicity using male rabbits, 24 hours under occlusive wrap with wet paste, LD50 of 10 g/kg (8.4 – 11.9 g/kg), III and with a 9% solution, LD50 of 2.2 g/kg (1.2 – 3.9 g/kg), category III. Page 10 states that signs at lethal doses were tremors and nasal discharge. 5. Sensitization with guinea pigs using 10 intradermal injections of 0.1 ml of 0.1% solution with a challenge was negative. 6. Standard plate incorporation *Salmonella* assay at 0.1 to 500 ug/plate with and without activation was negative with toxicity at >100 ug/plate. The above assays were also run with the "use" material and found to be nontoxic (page 11). The authors state that trichloromelamine had not been tested for carcinogenicity up to that date. Appendices contained individual data. No worksheet. SUPPLEMENTAL. (Gee, 1/26/01)

51006-007 115401 "Skin permeability theory in relation to measurements of percutaneous absorption in toxicology" (Dugard, P. H., in: Dermatoxicology. Third edition, F. N. Marzulli and H. I. Maibach, eds., 95-120 (19??) A general discussion with no specific data. No worksheet. (Gee, 1/29/01)

001 045337 One paragraph summary of studies with melamine. No worksheet. (Gee, 1/30/01).